REMARKS

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Claims 1, 2, 4, 5, 9, 10, 12, 16-19 and 22-23 have previously been canceled without prejudice or disclaimer.

Claims 20 and 40-49 are withdrawn from consideration.

Claims 3, 6-8, 11, 13-15, 21 and 50-51 are under consideration in this application.

Applicants acknowledge in the Office Action of April 24, 2003, allowance of claim 11, and the allowance by rejoinder of process claims 13-15 and 21 in keeping with procedures set forth in the Official Gazette notice of March 26, 1996 (1184 O.G. 86) in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b). Additionally, Applicants acknowledge that the Examiner has withdrawn the written description rejection of claims 3, 6-8 and 11 under 35 U.S.C. § 112, first paragraph pertaining to fragments and percent identity of SEQ ID NO:1 and SEQ ID NO:2.

Rejoinder of Method Claims

Applicants reiterate that upon allowance of product claim 3, there should be rejoinder of "method of use" claims 6-8, 50 and 51, in accordance with the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)."

Amendments to the Claims

Claim 3 has been amended in order to further define the claimed invention. In particular, claim 3 d) has been amended to include the recitation of "an immunogenic fragment of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1, said immunogenic fragment is used to make an antibody which specifically binds to an isolated polypeptide selected from the group consisting of a), b) and c)." Support for this amendment can be found throughout the specification, e.g., p. 8, lines 16-19, p. 9, line 28, through page 10, line 1, page 30, lines 7-9 and page 52, lines 25-28. No new

matter is added by this amendment. It is believed that entry of the requested amendment is proper and would put the claimed invention in condition for allowance or in better form for appeal.

Claims 50 and 51 have been added as "method of use" claims of the polynucleotide of SEQ ID NO:2 encoding the polypeptide of SEQ ID NO:1. Support for these claims can be found throughout the Specification, e.g., page 5, lines 2-7, and page 22, line 20 through page 28, line 4. No new matter is added by this amendment. It is believed that entry of the requested amendment is proper and would put the claimed invention in condition for allowance or in better form for appeal.

Improper Final Rejection

Applicants respectfully request the withdrawal of the Finality of this Office Action since the issue as to an "immunogenic fragment" is a new ground of rejection since it was not included as part of the rejection of claims 3 and 6-8 as allegedly lacking an adequate written description under 35 U.S.C. § 112, first paragraph in the Office Action of August 29, 2002.

In the Office Action of August 29, 2002, the reasons given in support of the rejection of claims 3 and 6-8 for insufficient written description addressed only the recitation of 90% variants of SEQ ID NO:1 and SEQ ID NO:2 and the function of the polypeptide:

- there is insufficient written description as to the identity of a polypeptide having at least 90-99% sequence identity to SEQ ID NO:1 or a polynucleotide that would be 90-99% identical to SEQ ID NO.2 and that would still maintain the function of the polypeptide. Consequently the specification does not provide an adequate written description of a polypeptide having at least 90-99% sequence identity to SEQ ID NO:1 a polynucleotide that would be 90-99% identical to SEQ ID NO.2 and that would still maintain the function of the polypeptide (Office Action at page 3).

Accordingly, it was assumed that there was an adequate written description under 35 U.S.C. § 112, first paragraph for the recitation of an "immunogenic fragment". Applicants therefore request that the Status of the Office Action issued on April 24, 2003 be made Non-final as a matter of record.

In the interest of expediting prosecution, however, Applicants will address the issue of an "immunogenic fragment" as requested in this Office Action. Further, Applicants respectfully request consideration and entry of the amendments to claim 1d) and consideration of the arguments that follow

as to why Applicants assert that there is an adequate written description under 35 U.S.C. § 112, first paragraph for the recitation of an "immunogenic fragment" as now claimed in claim 1d), since this is the first time the Examiner has raised this issue and is thus a new ground of rejection.

Written Description Rejection Under 35 U.S. C. § 112, first paragraph

Claims 3 and 6-8 stand rejected under U.S.C. § 112, first paragraph, for the reason given at page 3 of this Office Action. Applicants traverse this rejection for the reasons that follow.

A. Legal Requirements

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics[42] which provide evidence that applicant was in possession of the claimed invention,[43] i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.[44] What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.[45] If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met.[46]

Moreover, according to the Manual of Patent Examining Procedure, evaluation of the Specification's disclosure showing that applicant was in possession of the claimed invention is a multi-factorial determination.

> Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. (M.P.E.P. 2163 II. A. 3. (a) i) (C) (2), emphasis added).

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

B. The Specification provides an adequate written description of the claimed "immunogenic" term as it relates to fragments of SEQ ID NO:1

The subject matter encompassed by claims 3 and 6-8 is adequately disclosed in the Specification given what is conventional or well known to one skilled in the art.

Please note that the "immunogenic" language of independent claim 3 as amended recites:

3. **(Three Times Amended)** An isolated polynucleotide encoding a polypeptide selected from the group consisting of: . . .

d) an immunogenic fragment of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1, said immunogenic fragment is used to make an antibody which specifically binds to an isolated polypeptide selected from the group consisting of a), b) and c).

Applicants submit that the Specification provides an adequate written description of the claimed polynucleotide encoding a polypeptide consisting of an "immunogenic" fragment of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1 to convey with reasonable clarity to those skilled in the art that applicant was in possession of the invention as claimed at the time of the filing of this application.

The Examiner's position is that although the Specification provides an adequate written description of the polypeptide of SEQ ID NO:1, fragments and 90-99% variants thereof as well as the polynucleotide of SEQ ID NO:2, fragments and 90-99% variants thereof, adequate written description of "immunogenic" is lacking (Office Action of April 29, 2003 at pages 2-3). Applicants strongly disagree with this position.

The structure of the "immunogenic" fragments is defined in terms of the amino acid sequence of the SEQ ID NO:1 (PDE9A) polypeptide and fragments thereof to which antibodies would be made and specifically bind. The Specification defines and one of skill in the art understands "immunogenic" fragments as those fragments which have the capability to be "immunologically active . . . the capability of the natural, recombinant, or synthetic PDE9A, or any oligopeptide thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies" (Specification, page 9, line 28 through page 10, line 1).

The Specification teaches SEQ ID NO:1 as provided in Figures 1A-1F, 2A-2D and in the Sequence Listing, pages 54-56. Moreover, methods of identifying immunogenic regions and so, immunogenic fragments of SEQ ID NO:1 are also provided in the Specification. Specifically, the DNASTAR software suite includes the LASERGENE program. Such software programs are well known to one of ordinary skill in the art and are routinely used to identify antigenic ("immunogenic") regions, including "an immunogenic" fragment of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1" (See, for example, Example XI, pages 52-53). Given the information provided by SEQ ID NO:1 (the amino acid sequence of PDE9A) and SEQ ID NO:2 (the polynucleotide sequence encoding PDE9A), one of skill in the art would be able to routinely obtain "an immunogenic fragment of at least 5 amino acids of a polypeptide having the amino acid sequence of SEQ ID NO:1" as recited in claim 3. Further, the skilled artisan knows that within the protein or fragments thereof which are used to immunize a host animal there exist numerous regions (the immunogenic (antigenic) fragments) which may induce the production of antibodies.

Additionally, the Specification teaches methods of making antibodies using oligopeptides, peptides, or fragments of PDE9A which consist of at least 5 amino acids of SEQ ID NO:1 (See, for example, page 29, line 25 through page 31, line 10 and Example XI, pages 52-53). Thus, one skilled

in the art need not make and test vast numbers of "immunogenic" fragments of SEQ ID NO:1. Instead, one of skill in the art need only analyze the polypeptide sequence of SEQ ID NO:1 for "immunogenic" regions, as described above. Further, because the art is very advanced, it is well known to one of skill in the art that antibody production requires routine experimentation in order to determine which "immunogenic" regions of a polypeptide or fragment thereof, result in an antibody with the desired antipeptide activity. The Specification also provides an assay (Example XI) for optimizing selection of immunogenic fragments of SEQ ID NO:1 used to make PDE9A specific antibodies. Likewise, the Examiner should note and one of skill in the art would recognize that antibodies made from such "immunogenic" fragments of SEQ ID NO:1 which specifically bind to the PDE9A polypeptide can be used to purify PDE9A from media containing PDE9A as taught in Example XII (page 53). Therefore, Applicants have provided an adequate written description of "immunogenic" fragments of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1 in terms of the structure of SEQ ID NO:1, use of sequence analysis programs well known to one of skill in the art and assays for producing and testing antibodies made with said "immunogenic" fragments (Examples XI and XII).

When provided with the detailed description as noted above, one of ordinary skill in the art "would have understood the inventor to be in possession of the claimed invention at the time of filing." That is, given the polypeptide sequence of SEQ ID NO:1 and the appropriate software program for the analysis of antigenic regions of a polypeptide, it would be routine for one of skill in the art to recognize whether a fragment of a polypeptide of SEQ ID NO:1 was "immunogenic." Accordingly, the Specification, together with what is conventional or well known to one of ordinary skill in the art, provides an adequate written description of "an immunogenic fragment of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1."

Applicants submit that "a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing" as stated in the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001. Accordingly, claims 3 and 6-8 meet the statutory requirements for written description under 35 U.S.C. 112, first paragraph. For at least the above reasons it is requested that this rejection be withdrawn.

C. Conclusion

The Office Action failed to base its written description inquiry "on whatever is now claimed." Consequently, the Action did not provide an analysis of the present claims. In particular, the "immunogenic" fragments of SEQ ID NO:1 are adequately described, as evidenced by the advanced nature of the art, the skill of the ordinary artisan and the specific passages of the Specification as set forth above. In addition, the Office Action of August 29, 2002 provided no analysis of why one of ordinary skill in the art would not have understood from the disclosure in the Specification along with "[w]hat is conventional or well known to one of ordinary skill in the art," that Applicants were in possession of "immunogenic" fragments of a polypeptide of at least 5 amino acids of the amino acid sequence of SEQ ID NO:1. Therefore, the Examiner has issued a new ground of rejection and improperly issued a Final Office Action on April 24, 2003.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney/Agent below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108**, as set forth in the enclosed fee transmittal letter.

Respectfully submitted,

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IN THE CLAIMS:

Claims 48 and 49 have been cancelled.

Claims 50 and 51 have been added.

Claim 3 has been amended as follows:

3. **(Three Times Amended)** An isolated polynucleotide encoding a polypeptide selected from the group consisting of:

a.) a polypeptide comprising the amino acid sequence of SEQ ID NO:1,

b) a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said polypeptide having cyclic nucleotide phosphodiesterase activity,

c) a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1, said fragment having cyclic nucleotide phosphodiesterase activity, and

d) an immunogenic fragment of a polypeptide [having] <u>of at least 5 amino acids of</u> the amino acid sequence of SEQ ID NO:1<u>, said immunogenic fragment is used to make an antibody which specifically binds to an isolated polypeptide selected from the group consisting of a), b) and c)</u>.

50. **(New)** A method of producing a polypeptide of claim 3, the method comprising:

a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 1, and

b) recovering the polypeptide so expressed.

51. **(New)** A method of claim 50, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:1.